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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

In re PATENT APPLICATION OF

WEINBERG et al — Atty. Ref.: 1579-21

Serial No.: 08/753,851 — Group Art Unit: 1644

Filed: December 2, 1996 — Examiner: Gambel, P.

For: A METHOD OF INHIBITING HIV INFECTION

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January 2, 2002

APPEAL BRIEF

Hon. Commissioner of Patents
and Trademarks
Washington, DC 20231

Sir:

This is an appeal from the final rejection of claims 9-12, 14-19 and 23-25.

REAL PARTY IN INTEREST

The real party in interest in this application is Duke University of Durham, North Carolina.

RELATED APPEALS AND INTERFERENCES

No other appeals or interferences are known to Appellants, Appellants' legal representative, or assignee which will directly

affect or be directed affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF THE CLAIMS

Claims 9-12, 14-19 and 23-25 are pending in and have been considered in this application. No claim stands allowed. Claims 1-7 were cancelled in the Amendment filed December 23, 1993. Claim 8 was cancelled in the Amendment filed March 10, 2000. Claim 13 was cancelled in the Amendment filed April 22, 1996. Claim 20 was not entered and claims 21 and 22 were cancelled in the Amendment filed April 1, 1999. The claims on appeal are set forth in the attached Appendix.

STATUS OF THE AMENDMENTS

The claim revisions proposed in the Amendment under Rule 116 filed March 10, 2000, have been entered and the request for reconsideration set forth in the Amendment Under Rule 116 filed August 30, 2001, has been considered.

SUMMARY OF THE INVENTION

In one embodiment, the present invention (as claimed in claim 16 and claims depending therefrom) relates to a method of inhibiting CD44-facilitated HIV infection of a mononuclear phagocyte susceptible to infection with a strain of HIV. The method comprises contacting the mononuclear phagocyte with an amount of an agent that binds to CD44 molecules present on the surface of the mononuclear phagocyte and thereby inhibits the CD44-facilitated infection of the mononuclear phagocyte.

In another embodiment, the present invention (as claimed in claim 23) relates to a method of reducing HIV infection or expression in normal human monocytes. This method comprises contacting the monocytes with an effective amount of an anti-CD44 antibody.

In a further embodiment, the present invention (as claimed in claim 24) relates to a method of effecting post HIV exposure prophylaxis therapy comprising administering to an individual in need of such therapy an effective amount of an anti-CD44 antibody.

Support for the invention as claimed can be found, for example, at pages 29-30 and in the working Example at page 31.

The foregoing represents a concise summary of the invention.

THE ISSUES

Claims 9-12, 14-19 and 23-25 stand rejected under 35 USC 112, first paragraph, as the subject specification allegedly fails to teach how to make and/or use the invention.

Claims 14-19 also stand rejected under 35 USC 112, first paragraph, as it is allegedly being non-enabled.

Accordingly, the issues presented for review are:

i) whether the subject matter of claims 9-12, 14-19 and 23-25 is enabled by the disclosure; and

ii) whether the subject matter of claims 14-19 is enabled by the disclosure.

GROUPING OF THE CLAIMS

For each ground of rejection that applies to two or more claims, those claims stand or fall together.

THE ARGUMENTS

i) Rejection of claims 9-12, 14-19 and 23-25 under 35 U.S.C. §112, first paragraph. The Examiner's rejection of the

claims as non-enabled is submitted to be in error for the reasons that follow.

The invention described and claimed in the above application results from Appellants' finding that CD44 (the haluronate receptor) facilitates HIV infection in human cells. When CD44 is blocked by binding to an anti-CD44 antibody, there is a 40-80% reduction of HIV infection/expression in human monocytes *in vitro*. Appellants disclose in the subject application that the natural ligand of CD44, haluronate or haluronic acid, inhibits infection/expression up to 85%. In contrast, chondroitin sulfate, a polyanion that does not bind CD44, reportedly has little if any inhibitory activity.

The Weinhold Declaration of record makes clear the background against which the present invention was made and the technical basis for Appellants' assertions regarding predictability of efficacy *in vivo*, given the available data.

Declarant Weinhold points out that the ability to block HIV infection of mononuclear phagocytes using CD44 blocking agents is of obvious significance. Mononuclear phagocytes are concentrated in the mucosa (for example, the vaginal mucosa) and thus are important target cells. Declarant Weinhold indicates that from a therapeutic standpoint, these target cells are readily accessible. That is, the CD44 blocking agent can be administered

topically to the mucosal surface or, for example, within a condom. The application in fact makes specific reference to loco-regional (e.g., intravaginal) administration. Alternatively, the blocking agent can be administered parenterally.

Declarant Weinhold comments that the concept underlying the invention is a straightforward one and indicates that he sees little reason to doubt the effectiveness of the approach. Declarant Weinhold goes on in paragraphs (5) and (6) of his Declaration to provide basis for his view in this regard.

It is submitted that the Examiner has not given proper weight to this Declaration. Indeed, he has essentially dismissed the Declarant's statements with the unsupported comment "such studies do not necessarily correlate with inhibiting CD44-facilitated HIV infection…". Clearly the Declarant, one highly skilled in the relevant art, has a different view.

As regards the Examiner's comments relating to Rivadeneira et al, those comments are believed to miss the point of the present invention. Mononuclear phagocytes are of great importance in the cell to cell transmission of the virus. It is clear on its face that blocking such transmission is therapeutically significant. While the Examiner's comments

suggest that he takes a different view, he has not provided support for his position.

The Examiner's comments overlook the fact that a patent applicant enjoys the presumption that the invention can be practiced as claimed. The burden is on the examiner to provide evidence or reasoning inconsistent with the disclosure as to why such would not be the case. The broad brush assertions made by the Examiner do not constitute such evidence or reasoning.

Reversal is requested.

ii) Rejection of claims 14-19 under 35 USC 112, first paragraph. The rejection is in error and should be reversed for the reasons that follow.

Claim 16, from which the remaining claims depend, is drawn to a method of inhibiting CD44-facilitated HIV infection of a mononuclear phagocyte. The claim is not drawn to an agent that binds CD44 molecules present on the cell surface. As indicated above, it was Appellants that discovered, and disclose in the subject application, that CD44 facilitates HIV infection in humans. Given the nature of their contribution, it is entirely appropriate they be entitled to a method claim that covers the use of any and all agents that bind CD44 and in so doing block HIV infection. The Examiner has not provided basis for his position that, in situations such as this, specific

characterizing information is required for all agents that serve the intended purpose in the context of the claimed method.

To require that Appellants' method claims be limited to any particular agent would be to unduly restrict Appellants in the scope of protection to which they are rightly entitled. Reversal is requested.

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The Examiner's rejections under 35 USC 112 are not well founded for the foregoing reasons and reversal of same is requested.

Respectfully submitted,

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APPENDIX

9. The method according to claim 16 wherein said agent is selected from the group consisting of an anti-CD44 antibody, soluble CD44, CD44 oligopeptides and hyaluronate.

10. The method according to claim 8 wherein said agent is a CD44 oligopeptide selected from the group consisting of CD44-1 (SEQ ID NO:1), CD44-2 (SEQ ID NO:2), CD44-3 (SEQ ID NO:3), CD44-4 (SEQ ID NO:4), CD44-5 (SEQ ID NO:5), CD44-6 (SEQ ID NO:6), CD44-6a (SEQ ID NO:7), CD44-7 (SEQ ID NO:8), CD44-8 (SEQ ID NOS: 9, 10 AND 11), CD44-9 (SEQ ID NO:12), CD44-10 (SEQ ID NO:13), CD44-11 (SEQ ID NO:14), CD44-12 (SEQ ID NO:15), and CD44-13 (SEQ ID NO:16).

11. The method according to claim 16 wherein the agent is anti-CD44 antibody A3D8.

12. The method according to claim 16 wherein said agent is hyaluronate.

14. The method according to claim 16 wherein said phagocyte is a human monocyte.

15. The method according to claim 16 wherein said infection is HIV-1 infection.

16. A method of inhibiting CD44-facilitated HIV infection of a mononuclear phagocyte susceptible to infection with a strain of HIV comprising contacting said mononuclear phagocyte with an amount of an agent that binds to CD44 molecules present on the surface of said mononuclear phagocyte and thereby inhibit said CD44-facilitated infection of said mononuclear phagocyte by said strain of a HIV.

17. The method according to claim 16 wherein said mononuclear phagocytes are vaginal cells.

18. The method according to claim 16 wherein said contacting is effected by topical administration.

19. The method according to claim 16 wherein said cells are *in vitro* mononuclear phagocytes.

23. A method of reducing HIV infection or expression in normal human monocytes comprising contacting said monocytes with

an effective amount of an anti-CD44 antibody.

24. A method of effecting post HIV exposure prophylaxis therapy comprising administering to an individual in need of such therapy an effective amount of an anti-CD44 antibody.

25. The method according to claim 16 wherein said strain of HIV is a monocytotropic strain.